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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/774,248

02/06/2004

Joel A. Bader

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06/16/2005

USDA-ARS-OFFICE OF TECHNOLOGY TRANSFER
NATIONAL CTR FOR AGRICULTURAL UTILIZATION RESEARCH
1815 N. UNIVERSITY STREET
PEORIA, IL 61604

EXAMINER

ZEMAN, ROBERT A

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/774,248

Applicant(s)

BADER ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

The amendment and response filed on 3-21-2005 are acknowledged. Claims 1 and 4 have been amended. Claims 1-9 are pending and currently under examination.

Claim Objections Maintained.

The objection to claim 7 for starting with the improper article is maintained for reasons of record. As outlined previously, dependent claims should start with the article "the". Use of the article "a" suggests that more than one method is recited in the parent claim. Appropriate correction is required. It should be noted that Applicant did not address this objection in his response.

New Objections

The amendment filed 3-21-2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: the term "CFU/ml" does not appear to have support in the specification. The portion of the specification cited by Applicant is drawn to the analysis of assay results not the concentration of the initial doses. Consequently, said term is deemed to be new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections Maintained

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase “strain of *Flavobacterium columnare* is selected from the group consisting of NRRL B-30687” is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 2 and 4 under 35 U.S.C. 112, first paragraph, for failing to comply with the biological deposit requirements is maintained for reasons of record. Applicant's declaration with regard to the removal of all restrictions on the availability of NRRL B-30687 is noted. However, this statement is insufficient to overcome the aforementioned rejection.

As outlined previously, it is apparent that the bacterial virus strains represented by the Agricultural Research Service Culture Collection in Peoria, Illinois, USA under the deposit number NRRL B-30687 is required in order to practice the invention. The deposit of biological organisms is considered by the Examiner to be necessary for the enablement of the current invention (see 37 CFR 1.808(a)). The examiner acknowledges the deposit of organisms under the deposit number NRRL B-036087 under the provisions of the Budapest Treaty in partial compliance with this requirement (see page 5 of the specification). However, said deposits are not in full compliance with 37 CFR 1.803-1.809.

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If the deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See **37 CFR 1.808**.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit, or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

- 1) During the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;
- 2) All restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; and
- 3) **The deposits will be maintained for a term of at least thirty (30) years from the date of the deposit or for the enforceable life of the patent or for a period of at least five (5) years after the most recent request for the furnishing of a sample of the deposited material, whichever is longest; and**
- 4) **A viability statement in accordance with the provisions of 37 CFR 1.807; and**
- 5) **The deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.**

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 – 1.809 for additional explanation of these requirements.

The rejection of claims 1, 3 and 5-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for attenuated, ampicillin resistant *Flavobacterium columnare* which is effective for eliciting a protective immune response in fish against virulent strains of *Flavobacterium columnare* wherein the protective bacteria is *Flavobacterium columnare* strain NRRL B-30687, does not reasonably provide enablement for any other attenuated strains of *Flavobacterium* or their use as a vaccine against virulent strains of *Flavobacterium* in fish is maintained for reasons of record. The specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues:

1. The rejected claims are clearly limited to attenuated strains of *F. columnare* that are effective for eliciting a protective immune response in fish against virulent strains of *F. columnare*.
2. The instant claims, as amended, are limited to those attenuated, ampicillin resistant strains of *Flavobacterium columnare* characterized by smooth-edged colonies and significantly less ability to adhere to skin tissue than the parent, non-attenuated strain of *Flavobacterium columnare*.
3. The specification discloses the high degree of correlation of smooth-edged morphology and skin adhesion with a protective immune response.
4. The mechanism of protection is not necessarily an antigen-antibody response; said mechanism may simply be that the mutant blocks adherent sites for attachment of virulent *F. Columnare*.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion, the specification does not provide a high degree of correlation of smooth-edged morphology and skin adhesion with a protective immune response. The specification discloses a single species of attenuated, ampicillin resistant strains of *Flavobacterium columnare* characterized by smooth-edged colonies and significantly less ability to adhere to skin tissue than the parent, non-attenuated strain of *Flavobacterium columnare* (*Flavobacterium columnare* strain NRRL B-30687). The specification is silent as to the efficacy

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of any other strains of *F. columnare* that meet the aforementioned limitations. Consequently, one of skill in the art to make and use the claimed invention without undue experimentation.

With regard to Point 4, not knowing the mechanism of action, makes predicting the efficacy of a given *F. columnare* strain more difficult.

As outlined previously, the rejected claims are drawn to attenuated, ampicillin resistant strains of *Flavobacterium columnare* characterized by smooth-edged colonies and significantly less ability to adhere to skin tissue than the parent, non-attenuated strain of *Flavobacterium columnare* that are effective for eliciting a protective immune response against virulent strains of *Flavobacterium* and methods for their prophylactic use. To be a prophylactic composition, the composition must elicit protective immunity, demonstrable by pathogen challenge experiments in a reasonable model system. The specification, as filed, does not demonstrate that any *Flavobacterium* species, other than strain NRRL B-30687, provides any sort of protective immunity against virulent *Flavobacterium* in fish. Applicant describes a method of inducing immunity to virulent *Flavobacterium* in fish in a prophetic sense but fails to demonstrate said immunity can be achieved using any other attenuated, ampicillin resistant strains of *Flavobacterium columnare*. Moreover, Applicant has described a process of selection based on increased resistance to ampicillin but has provided no guidance as to which particular *Flavobacterium columnare* proteins are altered in said selection process. Applicant discloses that two proteins of approximately 40kDa and 50kDa differ in the "selected" attenuated strain (NRRL B-30687) as compared to the wild type *Flavobacterium columnare*, yet said proteins are not identified. Additionally, no genetic analysis has been done on the selected strain. Therefore,

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the skilled artisan has no way to predict *a priori* whether a given *Flavobacterium columnare* strain would be useful as a vaccine. Additionally, the skilled artisan would have no way of knowing whether any other ampicillin resistant *Flavobacterium columnare* strain selected as described in the specification would *necessarily* be attenuated and confer protective immunity.

Protective immunity is based on the ability of an organism to produce antibodies that aid in the elimination of a pathogen from said organism. Antibodies specifically bind to given "immuno-epitopes" of the antigen and while all proteins can, under the right circumstances, induce the production of antibodies, proteins with differing amino acid sequences will induce different antibodies. It is impossible to predict which proteins will induce protective antibodies, since the change of a single amino acid in the protein sequence of the antigen can effectively abolish the interaction between an antigen and an antibody (Colman, Res. Immunology, Jan 1994, Vol. 145, pages 33-36; e.g. page 33, column 2). Since a difference in even a single amino acid could radically affect the ability of a given antigen to induce protective immunity, in absence of evidence that the all antigens presented by the strains of *Flavobacterium columnare* have identical amino acid sequences, one would not be able to predict protective-immunity (or cross immunity). Consequently, while the skill in the art of immunology is high, to date, prediction of protective immunity for any given composition in any given animal is quite unpredictable. Given the lack of success in the art, the lack of description of the immuno-protective epitopes of *Flavobacterium columnare*, the lack of working examples and the unpredictability of the generation of protective immunity, the specification, as filed, does not provide enablement for the full scope of the rejected claims.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the phrase “significantly less ability to adhere to skin tissue than the parent...”. It is unclear what is meant by said phrase since “significantly less” is not explicitly defined in the specification. What constitutes a “significant” reduction? As written, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Claims 2 and 4, which recite the limitation of *Flavobacterium columnare* strain NRRL B-30687, are free of the art of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
June 13, 2005



MARK NAVARRO
PRIMARY EXAMINER